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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,159	08/15/2001	Tania Kastelic	1556.0290000	9266

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	7

DATE MAILED: 08/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,159	KASTELIC ET AL.	
	Examiner	Art Unit	
	Celine Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence letter* .

DETAILED ACTION

Claims 1-14 are pending in the application.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-9 and 12-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The term "gene" in claims 4-9 and 12-14 is improperly described in the specification. Unlike prokaryotes, the eukaryotic "gene" encompasses regions that reside both 5' and 3' to the

coding regions (which regulate gene expression) and introns as well. In the present application, however, the term "gene" appears to refer to only the coding region of a protein in a reporter system in the specification. Clearly, this is not a complete description of such a gene. Applicants may overcome this rejection by using terminology that refers to or denotes only the coding region of said gene. Whatever terminology used by applicants must also enjoy support by the present specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-3, 10 and 11 the recitation of "in which a DNA expression system...and wherein the mRNA which codes for the protein...a mRNA instability sequence is contacted with a test compound" renders the claims indefinite because it is unclear if the "DNA expression system", "the mRNA" or the "mRNA instability sequence" is contacted with "a test compound." In addition, it is also unclear whether the DNA expression system would generate detectable signal in the presence of the test compound.

Regarding claims 3, 10 and 11, the recitation "a method for comparison of compounds which induce mRNA degradation" renders the claims indefinite because it is unclear what features of the compounds are compared. In other words, it is unclear whether the method compares the structure, function or nomenclature of the test compounds.

Regarding claim 4-7, 8, 9 and 12-14, the word "associated" renders the claims indefinite because it is unclear whether the "5' and 3' UTR" is native to the "gene" or from other genes and operably linked to coding sequence of the recited gene. The recitation of "expression control elements and DNA corresponding to at least one copy of a mRNA instability sequence" also renders the claims indefinite because it is unclear whether the "expression control elements" or "DNA" is "corresponding to at least one copy of a mRNA instability sequence."

Regarding claims 5, 7-9, 13 and 14, the recitation "a stably transfected cell line comprising a reporter gene" renders the claim indefinite because it is unclear whether the cell line is stably transfected with the reporter gene, or some other construct wherein the cell line further comprises the reporter gene.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: How to determine whether the compound affect mRNA stability.

Claim 11 provides for the use of a mRNA stabilizing compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 11 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 10, 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Banholzer et al., 1997 (AT1).

The claims are drawn to a method for identification of a compound which affect mRNA stability or comparing said compounds comprises the steps of contacting the test compound with a DNA expression system that comprises at least one copy of mRNA instability sequence; determine the expression level of protein encoded by the expression system; and compare the expression level with a control expression system that lacks the mRNA instability sequence (1-3). The claims are further drawn to said DNA expression system (4), a cell line stably transfected with said DNA expression system (5), an assay system comprises said expression system and said control expression system (6), and an assay system comprises two cell lines stably transfected with said expression system and said control expression system respectively (7). Claims 10, 12-14 are drawn to a compound which destabilizes mRNA. These are product by process claims which read on the product, in the present instance, a compound which destabilizes mRNA. Absent evidence to the contrary, the method by which the compound is

identified does not impart upon said compound a patentable distinction from another such compound.

Banholzer et al. disclose that rapamycin promotes degradation of IL-3 transcripts at posttranscriptional level via 3' UTR (see page 3257, 2nd col., 1st paragraph). Banholzer et al. disclose two cell lines stably transfected with IL-3 expression system either with (VD1-M1) or without (VD1-M1ΔAU) mRNA instability sequence (3' UTR) (see page 3256, 1st col., lines 1-3). Banholzer et al. also disclose that following rapamycin and FK506 treatment, endogenous and exogenous wild type IL-3 decayed with very similar kinetics (see Figure 3b, left panel) whereas the exogenous mutant IL-3 mRNA level is not affected by either compound (Figure 3b, right panel, and 3c). The method and assay system disclosed by Banholzer et al. identifies rapamycin and FK506 as compounds that induce mRNA degradation. Therefore, Banholzer et al. disclose the instant claimed inventions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Danner et al., 1998 (AS4)., in view of Maniatis et al. (1987).

The claims are drawn to a stably transfected cell line comprising a first reporter expression system comprising at least one mRNA instability sequence, a second control expression system comprising a reporter gene different than the one in the first reporter system but lack mRNA instability sequence, and an assay system comprising said cell line.

Danner et al. teach a cell line (HEK293) transfected with a wild type β2AR expression vector, a β-globulin expression vector and a chimeric expression vector comprising β-globulin and 3'UTR of β2AR (either with or without mRNA instability sequence. Danner et al. teach that β-globulin/ β2AR mRNA half-life decrease upon isoproterenol or forskolin stimulation whereas wild type β-globulin remains same (see page 3227, 1st col., 2nd paragraph, and Figure 7). However, Danner et al. do not teach that the cell line is stably transfected.

Maniatis et al. teach a method of stably transfecting mammalian cells.

It would have been obvious to one of ordinary skill in the art to stably transfect the cell line with two expression system as taught by Danner et al. The ordinary artisan would have been motivated to do so for the ease of use of said cell line so that one does not have to transfect the cell line every time a compound needs to be tested. The ordinary artisan would have reasonable expectation of success because of the teaching of Danner et al., who teach an assay system comprising a cell line comprising different reporter construct can be used to measure mRNA

stability in response to different compounds, and the teaching of Maniatis et al., who teach a method to stably transfect mammalian cells. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
August 26, 2002

JAMES KETTER
PRIMARY EXAMINER